Saudi Journal of Medicine and Public Health

https://saudijmph.com/index.php/pub

https://doi.org/10.64483/jmph-165

Outcomes of Levofloxacin-Based Regimens in Adults with Severe Community-Acquired Pneumonia Requiring ICU Admission: A Single-Center Retrospective Cohort From Jazan, Saudi Arabia

Ahmed Hakami [(1)], Amnah Numan [(1)], Shoroog Obaidullah[(2)], Shahad Numan [(3)], Ahmad Alharbi [(4)] , Hanan Hakami[(5)], Hanan Bakri[(6)], Nawal Hakami[(7)], Mousa Zamili[(8)], Abdulmajeed Alanazi[(9)], Munif Ayyashi [(10)], Ali Mohammed Qassim Hazzazi [(11)], Bashaer Abdullah Hakami [(6)], Yahya Jaber Hazazi[(6)], Rami Almalki[(12)]

(1) Abu Arish General Hospital, Jazan Health Cluster, Ministry of Health, Saudi Arabia,
(2) King Saud Medical City (KSMC), Ministry of Health, Saudi Arabia,
(3) College of medicine, Jazan University, Saudi Arabia,
(4) Buridah Central Hospital, Qassim Health Cluster, Qassim, Ministry of Health, Saudi Arabia,
(5) Salah Al-Din Health Care Center, Riyadh Second Health Cluster, Riyadh, Ministry of Health, Saudi Arabia,
(6) King Fahd Central Hospital, Jazan, Ministry of Health, Saudi Arabia,
(7) King Fahd Central Hospital, Jazan Health Cluster, Jazan, Ministry of Health, Saudi Arabia,
(8) Abu arish General Hospital, Jazan Health Cluster, Jazan, Ministry of Health, Saudi Arabia,
(9) Dumat Aljandal General Hospital, Aljouf Health Cluster, Aljouf, Ministry of Health, Saudi Arabia,
(10) Jazan Specialist Hospital, Jazan Health Cluster, Ministry of Health, Saudi Arabia,
(11) Abu-Arish General Hospital, Ministry of Health, Saudi Arabia
(12) King Faisal Hospital, Makkah Health Cluster, Makkah, Ministry of Health, Saudi Arabia

Abstract

Background

Levofloxacin is widely used in combination regimens for severe community-acquired pneumonia (CAP) in the ICU; however, real-world outcome data from resource-limited settings remain scarce.

Objective:

To evaluate 28-day mortality and key clinical/safety outcomes among adults with severe CAP requiring ICU admission who received levofloxacin-based regimens at Abu-Arish General Hospital.

Methods

We conducted a retrospective cohort study that examined patient data captured through an electronic medical system at the Abu Arish General Hospital between 2021 and 2022 (Single-center retrospective cohort (dates), Abu-Arish General Hospital ICU). We used the repeated measures ANCOVA to investigate the effect of Levofloxacin on a wide range of medical parameters. Data analysis was performed with SPSS statistics (Version 25).

Results

A total of 93 patients were included in this study. The study examined the impact of levofloxacin on various medical parameters, including age, weight, height, BMI, initial dosage, comorbid diseases and sex. The adjusted mean differences between before and after Levofloxacin administration revealed significant changes in a variety of medical parameters, including hepatic markers and hematologic indices.

Conclusion

Levofloxacin therapy can produce change in baseline clinical characteristics of critical ill patients in the intensive care unit. We need to investigate the tolerability of this therapy in terms the severity of side effects on a large sample of the critically ill patients in the future. This study
will allow healthcare providers to give better care to these patients.

Categories: Infectious Disease, Epidemiology/Public Health

Keywords: Hepatic markers, Hematologic indices, Levofloxacin

Introduction

The most common infectious diseases are the lower respiratory tract [1]. According to the World Health Organization (WHO), lower respiratory tract infections are the leading infectious cause of death globally, accounting for 3.5 million fatalities each year [2]. Pneumonia is the most common infectious disease of the lower respiratory tract infection [3]. The latest WHO data published in 2020 show that influenza and pneumonia deaths in Saudi Arabia reached 6,132 or 4.58% of total deaths [4]. Pneumonia is a source of morbidity and mortality, particularly in the elderly,

*Corresponding author e-mail Ahmed.Ali.Hakami@hotmail.com (Ahmed Hakami).

Receive Date: 12 September 2025, Revise Date: 30 Septembre2025, Accept Date: 19 October 2025

persons with weakened immune systems, and those with underlying medical issues [5]. It is an acute lung parenchyma infection caused by bacteria, viruses, and fungi [6][5]. The preferred treatment for bacterial pneumonia is an antibiotic [9]. Fluoroquinolones are authorized to treat bacterial illnesses, including pneumonia [11]. Levofloxacin is the most frequently used fluoroquinolone [11]. Levofloxacin is a broad-spectrum, third-generation fluoroquinolone and bactericidal antibiotic that directly inhibits the synthesis of bacterial DNA [12]. It promotes DNA strand breaks by preventing DNA-gyrase in vulnerable organisms from relaxing supercoiled DNA [12]. It treats Gram-positive, Gram-negative, and atypical pathogens like Streptococcus pneumonia, Haemophilus influenza, and Pseudomonas aeruginosa [13].

Levofloxacin is a popular empirical choice in treating severe pneumonia [13]. Antimicrobial pharmacokinetics are changed in critically ill patients, such as medication clearance, volume of distribution, and elimination half-life. [10]. The most common side effects of levofloxacin are tendinitis, tendon rupture, seizures, prolonged QT interval, peripheral neuropathy and hepatotoxicity [16][17]. A Study conducted in 2021 reported that there was a strong correlation between exposure to fluoroquinolone and the risk of acute aortic dissection [17]. A case report study published in 2021 showed that levofloxacin-induced pancreatitis when treating a patient with acute pancreatitis [19]. Another case report published in 2020 and 2023 showed levofloxacin-induced toxic epidermal necrolysis [21][22]. A literature review study conducted in 2023 reported that movement disorders (MD) were linked to fluoroquinolone [20]. Based on previous studies, none of these studies were performed in Saudi Arabia to show the impact of levofloxacin side effects in critically ill patients. Also, there is a limited study to evaluate the clinical result after using levofloxacin in a critically ill patients with pneumonia which is beneficial for healthcare providers to know how common these clinical results are among critically ill patients with pneumonia since this will allow them to give better care to their patients. We focus on severe community-acquired pneumonia (CAP) requiring ICU admission, a setting in which respiratory fluoroquinolones, including levofloxacin, are commonly used as part of initial combination therapy. Levofloxacin provides broad coverage of typical and atypical CAP pathogens, achieves high epithelial lining fluid concentrations, and permits early IV-to-PO transition when clinically appropriate. Evaluating outcomes associated with levofloxacin-based regimens in our ICU population addresses a practice-relevant question at Abu-Arish General Hospital and clarifies real-world effectiveness and safety in a resource-constrained setting.

Evaluating how often levofloxacin is used among critical care patients with pneumonia and its effect on the patient’s clinical characteristics are the main goals of our study. Other goals of this study are to determine the baseline traits of patients at the beginning of levofloxacin treatment and in patients following levofloxacin therapy. If this is performed, we will better understand the adverse effect of levofloxacin on the critical ill patients, lead to improved patients' safety and reduced fatality by collaboration of all healthcare providers and patients with others to improve patient outcomes with reduced risk of adverse drug reactions and increased patient satisfaction related to levofloxacin therapy.

The main aim is to evaluate clinical effectiveness and safety of levofloxacin-based regimens among adults with severe community-acquired pneumonia (CAP) requiring ICU admission, specifically assessing 28-day all-cause mortality (primary endpoint) and secondary endpoints (time to clinical stability, ICU and hospital length of stay, need/duration of invasive ventilation, vasopressor-free days, microbiologic response when available, and antibiotic-associated adverse events including C. difficile infection and QT-related events).

METHODOLOGY

Observational, analytical and retrospective cohort study was performed on all pneumonia patients who were treated with levofloxacin at Abu-Arish General Hospital 2021 and 2022 with a timeframe for two years (Single-center retrospective cohort (dates), Abu-Arish General Hospital ICU). The essential variables will be acquired from patients' health medical records at Abu-Arish General Hospital; hence we believe no informed consent will be necessary to get the data. The confidentiality of patients is ensured by assigning a code number to each of them. The patient information will be kept private and used only for research and analysis. Patients will never be contacted about the study's findings. The information gathered will be kept for one year. Although the results of this study may be published, the patients' identities will never be divulged.

Critically ill is defined as patients with an oxygen saturation of 94% or needing additional oxygen or mechanical breathing. All critically ill patients aged 18 years and over whose doctors’ recommended levofloxacin as a single drug or combination with other antibiotics for pneumonia between 2021 and 2022 were included. Patients under 18 years were excluded, as were cases where levofloxacin was prescribed for a condition other than pneumonia. Those who were not diagnosed with pneumonia or seriously unwell and those with non-critical illnesses were also excluded.

From 2021 to 2022, data will be collected from patient's medical records who take levofloxacin through the medical cloud care electronic system at Abu-Arish General Hospital in Jazan. The following data will be collected for the study, including demographic characteristics of patients, e.g., age, gender, smoking history, weight, height, levofloxacin

course completion, and the duration of levofloxacin (days). Also, the clinical characteristics of patients will be collected before and after levofloxacin use, including medical history (hypertension, diabetes, heart failure, and COVID-19 infection) and lab tests (liver enzyme (ALT and AST), leukocytosis, platelets, albumin, bilirubin, glucose, hemoglobin, level of SrCr (mmol/L) and Crcl). Patient identities, names, and medical record numbers will never be disclosed to protect patient's privacy. Data were reported as median and ranges, means, and standard deviations (SDs) for continuous variables. A chi-square test for association and analysis of variance (ANOVA) for mean differences were applied accordingly. All analyses were done at 5% significance using SPSS version 25.0.

Eligibility & cohort assembly:

From all ICU admissions during the study window, we screened adult patients (≥ 18 y) with a primary diagnosis of pneumonia and new lobar/interstitial infiltrate on chest radiograph or CT plus ≥ 1 compatible clinical feature (fever/hypothermia, leukocytosis/leukopenia, purulent sputum, or hypoxemia). We included only severe CAP (per above criteria) who received levofloxacin (IV or PO) within 24 hours of ICU admission as part of empiric therapy and for ≥ 48 hours unless death occurred earlier.

Exclusions: (1) HAP/VAP; (2) non-pneumonia primary infections (e.g., UTI, intra-abdominal, skin/soft-tissue, bacteremia without pulmonary source); (3) colonization without radiographic pneumonia; (4) pregnancy; (5) cystic fibrosis or bronchiectasis; (6) refusal of research authorization when applicable.

Statistical Analysis:

Descriptive statistics; multivariable regression for primary outcome; **(optional)** propensity-score analysis if a comparator exists; listwise deletion or multiple imputation strategy for missingness; two-sided $\alpha = 0.05$.

RESULTS

It is important to know first that operational definition of severe CAP requires ICU. Severe CAP was defined by ATS/IDSA criteria: ≥ 1 major criterion (invasive mechanical ventilation or septic shock requiring vasopressors) or ≥ 3 minor criteria (respiratory rate ≥ 30/min, $PaO_2/FiO_2 \leq 250$, multilobar infiltrates, acute confusion/disorientation, BUN ≥ 20 mg/dL, WBC < 4×10^9/L, platelets < 100×10^9/L, core temperature < 36 °C, or hypotension requiring aggressive fluid resuscitation). Patients meeting this definition and triaged to the ICU within 24 h of hospital arrival were eligible.

Levofloxacin is an antibiotic with a broad spectrum of action that is commonly used to treat bacterial infections. However, its impact on several medical indicators, such as total metabolic and hematologic profiles, are unknown. The objective of this investigation was to assess the influence of Levofloxacin on these parameters in a group of ninety-three patients who were administered the medication at varying dosages for varying amounts of time. The current study used repeated measures ANCOVA to investigate the effect of Levofloxacin on a wide range of medical parameters, as shown in Tables 2, 3, and 4. Age, weight, height, BMI, initial Levofloxacin dosage, and comorbid diseases (Table 3) were all carefully considered for adjustment to ensure a robust analysis. Table 4 contains significant adjustments for sex, recognizing its potential impact on the observed changes. The adjusted mean differences between before and after Levofloxacin administration revealed significant changes in a variety of medical parameters, including hepatic markers and hematologic indices.

Based on table 1's results, 93 individuals receiving levofloxacin treatment for a variety of infections were included in the study population. The patients' average age was 69.10 years (SD = 15.16), and their average weight was 70.31 kg (SD = 11.94). The average body mass index (BMI) was 26.39 kg/m^2 (SD = 7.56) and the average height was 164.72 cm (SD = 5.85). The average length of levofloxacin medication was 7 days (range = 1-30 days). The majority of patients (81.7%) were given a 500 mg initial dose, while 7.5% were given 250 mg and 10.8% were given 750 mg. There were 58.1% female and 41.9% male participants. None of the patients had a history of smoking or allergy. Hypertension was present in 75.3% of the patients, heart failure (HF) in 21.5%, diabetes mellitus (DM) in 41.9%, and COVID-19 infection in 46.2%. The mortality rate was 73.1%. Table 1 and figure 1-4 shows detail.

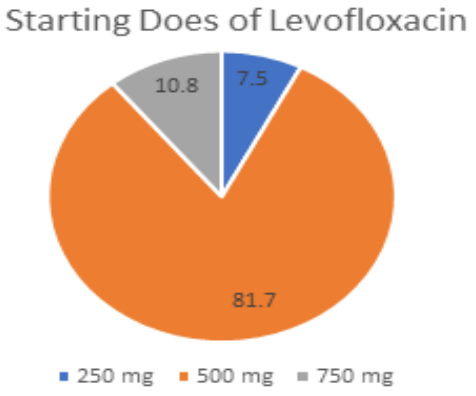

Figure 1: Starting Dose of Levofloxacin.

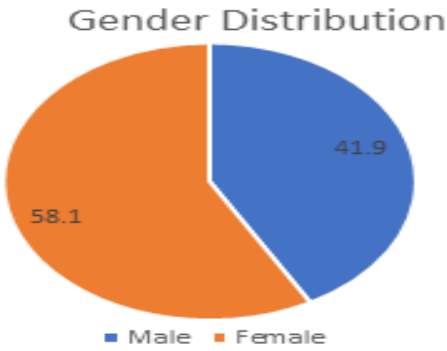

Figure 2: Gender Distribution of Participants

Table 1: *Sociodemographic and Clinical Characteristics of the Study Population (N = 93)*

Variable	*M/ n*	*SD/ %*
Age	69.10	15.16
Weight	70.31	11.94
Height	164.72	5.85
BMI	26.39	7.56
Duration on Levofloxacin*	7	18
Starting Dose		
250 mg	7	7.5
500 mg	76	81.7
750 mg	10	10.8
Gender		
Male	54	41.9
Female	39	58.1
Smoking History		
Yes	0	0.0
No	93	100.0
Allergy		
Yes	0	0.0
No	93	100.0
Hypertension		
Yes	70	75.3
No	23	24.7
HF		
Yes	20	21.5
No	73	78.5
DM		
Yes	39	41.9
No	54	58.1
COVID		
Yes	43	46.2
No	50	53.8
Dead		
Yes	68	73.1
No	25	26.9

Note. * Values are based on Median and Range of Days.

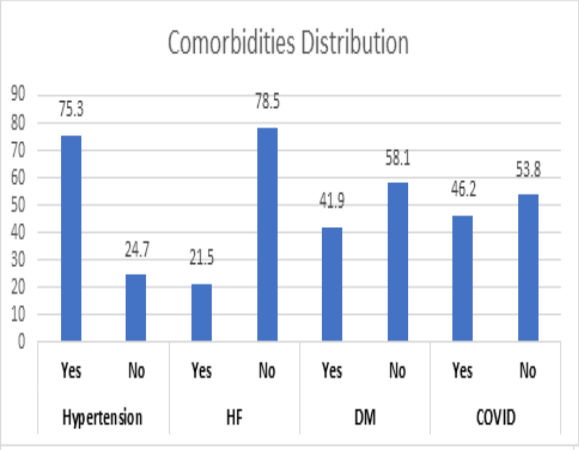

Figure 3: Comorbidities Distribution.

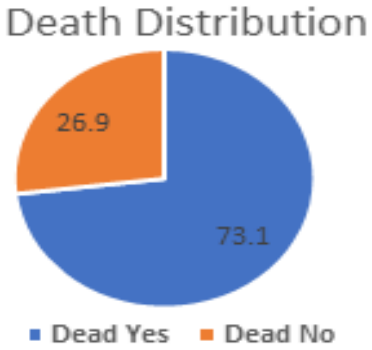

Figure 4: Death Distribution.

The findings of the repeated measures ANCOVA assessing the impact of Levofloxacin on medical parameters are presented in Table 2. Covariates, such as age, weight, height, BMI, and the initial dosage of levofloxacin, were taken into account for adjustment in the analysis.

Examining the adjusted mean differences between before and after Levofloxacin administration revealed significant changes in a variety of medical parameters. To begin with, bilirubin levels increased significantly from 16.48 (M) before to 29.87 (M) after Levofloxacin ($p<.001$). In a similar vein, ALT levels showed a significant rise, rising from 36.27 (M) to 120.55 (M) $p=.007$. Additionally, there was a significant increase in AST levels from 64.75 (M) to 364.33 (M) $p=.005$. Moreover, following Levofloxacin, Albumin levels dropped from 28.72 (M) to 26.66 (M) ($p=.011$). While potassium levels (K mmol/L) increased following Levofloxacin, the increase was not statistically significant (1.85, F, $p=.177$). Further the findings indicated that there was a significant increase in serum creatinine (SrCr) levels from 114.31 (M) to 205.59 (M) $p<.001$. Following the administration of Levofloxacin, there was no statistically significant change in the random blood glucose (RBG) levels ($p=.230$). Assessing Renal function, as measured by CrCr (ml/min), decreased significantly from 63.58 (M) to 51.19 (M), with a p value of.022. Likewise,

there was a significant drop in hemoglobin (HG) levels from 11.52 (M) to 9.73 (M) p <.001. In contrast to WBC counts, which increased significantly from 12.48 (M) to 16.49 (M) p <.001, platelet counts dropped significantly from 272.40 (M) to 184.86 (M) p <.001. The robustness of these findings is increased by the inclusion of covariates in the analysis, which highlights the significant impact of levofloxacin on a number of medical parameters. Table 2 shows detail.

The results from the repeated measures ANCOVA, evaluating the influence of Levofloxacin on medical parameters and incorporating covariates such as Comorbid Diseases (Hypertension, HF, Diabetes Mellitus, COVID), are elucidated in Table 3.

Table 2:*Covariates Adjusted Mean Difference Before and After Levofloxacin for Medical Parameters (Complete Metabolic and Hematologic Profile)*

Parameters	Before Levofloxacin (Adjusted)		After Levofloxacin (Adjusted)			
	M	***SE***	***M***	***SE***	***F***	***p***
Bilirubin UMOL/L	16.48	2.81	29.87	4.76	21.90	<.001
ALT U/L	36.27	6.17	120.55	30.97	7.72	.007
AST U/L	64.75	9.99	364.33	105.77	8.33	.005
Albumin g/dl	28.72	0.83	26.66	0.81	6.78	.011
K mmol/L	4.33	0.09	4.51	0.13	1.85	.177
SrCr(mmol/L)	114.31	6.75	205.59	16.72	35.53	<.001
RBG	9.40	0.57	11.37	1.56	1.46	.230
CrCr(ml/min)	63.58	3.50	51.19	5.10	5.47	.022
HG	11.52	0.27	9.73	0.26	66.58	<.001
Platelet	272.40	12.70	184.86	12.76	39.58	<.001
WBC	12.48	0.66	16.49	1.01	17.46	<.001

Note. Covariates were including Age, weight, Height, BMI, and Levofloxacin starting dose

Following Levofloxacin treatment, bilirubin levels showed a significant rise from 13.83 (M) to 32.10 (M) (p <.001). The levels of ALT, on the other hand, increased from 32.65 (M) to 113.37 (M), though this change was not statistically significant (p =.108). Parallel to this, AST levels increased numerically from 58.07 (M) to 292.77 (M), although the difference did not reach statistical significance (p =.184). Further, following the administration of Levofloxacin, albumin levels showed very little variation, with an extremely small adjusted mean difference of (p =.787). Potassium concentrations (K mmol/L) were relatively stable, with a non-significant adjusted mean difference of (p =.497).

In terms of renal function, serum creatinine levels increased significantly from 105.85 (M) to 193.44 (M) p.001. On the other hand, following Levofloxacin administration, random blood glucose (RBG) levels did not show a significant change (p =.445). Further, renal function, as measured by CrCr (ml/min), decreased significantly from 69.43 (M) to 48.90 (M) p =.019. Similarly, the levels of hemoglobin (HG) showed a significant decline from 11.51 (M) to 9.85 (M), p <.001. Moreover, the results also indicated a significant drop in platelet counts, from 249.52 (M) to 174.81 (M), p <.001. On the other hand, there was a significant increase in white blood cell (WBC) counts from 11.73 (M) to 17.97 (M) p <.001.

These results underscore the multifaceted impact of Levofloxacin on a range of medical parameters, accounting for comorbid diseases as covariates in the analysis. This comprehensive analysis provides valuable insights into the nuanced changes observed in response to Levofloxacin administration.

Table 3

Covariates Adjusted Mean Difference Before and After Levofloxacin for Medical Parameters (Complete Metabolic and Hematologic Profile)

Parameters	Before Levofloxacin (Adjusted)		After Levofloxacin (Adjusted)			
	M	***SE***	***M***	***SE***	***F***	***p***
Bilirubin UMOL/L	13.83	4.82	32.10	8.10	15.14	<.001
ALT U/L	32.65	10.46	113.37	50.91	2.63	.108
AST U/L	58.07	16.64	292.77	177.77	1.79	.184
Albumin g/dl	28.74	1.45	29.07	1.30	0.07	.787
K mmol/L	4.34	0.17	4.48	0.22	0.47	.497
SrCr(mmol/L)	105.85	12.28	193.44	28.67	12.58	<.001

RBG	8.42	0.87	10.57	2.73	0.59	.445
CrCr(ml/min)	69.43	6.53	48.90	8.57	5.73	.019
HG	11.51	0.42	9.85	0.40	21.88	<.001
Platelet	249.52	20.89	174.81	21.78	26.51	<.001
WBC	11.73	1.06	17.97	1.64	16.20	<.001

Note. Covariates were Comorbid Diseases including Hypertension, HF, Diabetes Miletus, COVID

The outcomes of the repeated measures ANCOVA investigating the effects of Levofloxacin on medical parameters, with Sex as the covariate, are elucidated in Table 4. After receiving Levofloxacin, bilirubin levels significantly increased (p <.001), rising from 16.48 (M) to 29.87 (M). ALT levels increased noticeably from 36.27 (M) to 120.55 (M), reaching statistical significance (p =.006). In the same way, AST levels showed a significant increase, rising from 64.75 (M) to 364.33 (M), with a statistical significance of p =.005.

In contrast, Albumin levels significantly dropped after Levofloxacin was administered (p =.009), going from 28.72 (M) to 26.66 (M). On the other hand, p =.177 indicates that there was no statistically significant change in potassium levels (K mmol/L). further, following Levofloxacin administration, serum creatinine levels showed a significant increase (p <.001), rising from 114.81 (M) to 205.59 (M). On the other hand, there was no statistically significant variation in random blood glucose (RBG) levels (p =.246).

Following Levofloxacin treatment, renal function as measured by CrCr (ml/min) significantly decreased, going from 63.58 (M) to 51.19 (M) (p =.019). Likewise, there was a noteworthy reduction in hemoglobin (HG) levels from 11.52 (M) to 9.73 (M) p <.001. Moreover, the results indicated a significant drop in platelet counts, from 272.40 (M) to 184.86 (M) p <.001. On the other hand, there was a noteworthy rise in white blood cell (WBC) counts, rising from 12.48 (M) to 16.49 (M) p <.001.

In conclusion, these findings illuminate the intricate impact of Levofloxacin on diverse medical parameters, accounting for Sex as a covariate in the analysis. This nuanced analysis provides valuable insights into the specific variations observed in response to Levofloxacin administration, while considering the influence of Sex on the results. Table 4 shows detail.

Table 4: *Covariates Adjusted Mean Difference Before and After Levofloxacin for Medical Parameters (Complete Metabolic and Hematologic Profile)*

Parameters	**Before Levofloxacin (Adjusted)**		**After Levofloxacin (Adjusted)**			
	M	***SE***	***M***	***SE***	***F***	***p***
Bilirubin UMOL/L	16.48	2.87	29.87	4.85	21.86	<.001
ALT U/L	36.27	6.11	120.55	30.33	8.04	.006
AST U/L	64.75	9.83	364.33	105.40	8.39	.005
Albumin g/dl	28.72	0.86	26.66	0.81	7.06	.009
K mmol/L	4.33	0.10	4.51	.13	1.85	.177
SrCr(mmol/L)	114.81	7.88	205.59	17.47	35.46	<.001
RBG	9.40	0.56	11.37	1.63	1.36	.246
CrCr(ml/min)	63.58	3.99	51.19	5.12	5.65	.019
HG	11.52	0.26	9.73	0.26	67.57	<.001
Platelet	272.40	12.54	184.86	12.85	38.28	<.001
WBC	12.48	0.66	16.49	1.00	16.89	<.001

Note. Covariate was Sex

DISCUSSION

Although fluoroquinolones are widely accepted as safe and well-tolerated antibiotics, they can have uncommon side effects and cause problems with the central nervous system, gastrointestinal tract, and blood [23]. One of the most often recommended fluoroquinolone antibiotics for respiratory tract infections, both inpatient and outpatient, is levofloxacin. It has a great safety profile and is usually well tolerated [23]. There are no reports of severe liver toxicity associated with levofloxacin use in English-language literature. Levofloxacin hepatotoxicity is supported by the time link between liver injury and levofloxacin administration, the quick decrease in liver enzyme levels following cessation, and the elevated liver enzyme levels prior to respiratory failure [23].

Levofloxacin has been linked in 2% to 5% of participants to mild increases in blood ALT and AST

levels in short-term studies. The problems were rarely dose-modifying and were often asymptomatic and transitory. Levofloxacin has been linked to at least 50 cases of clinically evident liver impairment due to its widespread use; these cases are primarily single case reports [30].

Levofloxacin is normally given for 7 days with critically ill patients. In our study, 81.7% of the patients received 500 mg levofloxacin and 73.1% of the patients died during the treatment course as a result of levofloxacin's side effects. The results of this investigation showed that levofloxacin administered orally significantly increased the activities of ALT, AST, and bilirubin. Serum AST and ALT are trustworthy indicators of liver integrity and function. High serum or plasma levels of AST, ALT, and bilirubin are typically suggestive of liver injury in both people and animals, according to prior researches [24]. When considering continuous variables in our study, such as age, weight, height, BMI, the initial dosage of levofloxacin and incorporating sex as a confounding variable, our study reported a statistically significant increase in bilirubin levels (p<.001), ALT levels (p =.007), AST levels (p =.005) and significant decrease in albumin levels (p =.011). While when incorporating comorbid diseases (hypertension, HF, diabetes mellitus and COVID-19 infection) as confounding variables, the significant change was found with increased bilirubin level (p <.001), serum creatinine levels increased significantly (p <.001) and CrCr significantly decreased (p =.019).

Our results were consistent to previous studies which have also reported hepatic injury after oral administration of levofloxacin for 3-10 days [23],[24]. Also, the results were consistent with case report included in previous study who experienced severe hepatic injury from fluoroquinolones, causing dramatic serum aminotransferase elevations within days of starting levofloxacin. The patient's death from multiorgan failure and subsequent pulmonary difficulties after making a full recovery raises the possibility that the injury played a role in chronic obstructive pulmonary disease of the patient [29]. The possible mechanisms include the production of reactive radicals in the liver during drug metabolism, which causes DNA damage, mitochondrial damage, and gene regulation leading to hepatocellular damage, may be the mechanism by which fluoroquinolones cause hepatotoxicity. This was seen in mice treated with levofloxacin, which increases hepatic mitochondrial peroxynitrite stress and disrupts the regulation of crucial mitochondrial enzymes and genes due to underlying elevated basal levels of super oxide. This process may be related to the DNA damaging mechanism of action of fluoroquinolones [24].

Our study revealed a significant drop in albumin levels after administration of levofloxacin (p =.011). Our results were almost similar to earlier studies, which have also reported that levofloxacin caused a considerable drop in albumin levels [25]. The most sensitive biomarker that is directly related to the degree of liver damage and toxicity is albumin [25].

We found a significant increase in serum creatinine (SrCr) levels (p <.001). Also, when assessing renal function, as measured by CrCr (ml/min), decreased significantly (p value .022). Serum creatinine concentration and clearance are often used to screen for renal function because creatinine is a metabolic waste product that is freely filtered by the kidneys' glomeruli. According to the results of previous study, levofloxacin taken orally raised creatinine levels significantly. The reduced GFR may be the primary cause of the elevated serum creatinine, or it may be secondary to the rise in reactive oxygen species [26], [27]. Our findings were inconsistent with those of a prior study that found decreased renal function cannot account for the apparent lack of an independent effect of critical illness on levofloxacin pharmacokinetics [13].

Our study revealed a significant drop in hemoglobin (HG) levels from (p <.001), a significant increase in WBC counts (p <.00) and platelet counts dropped significantly (p <.001), these significant changes were found with both the continuous variables and the confounder variables. Our results were consistent with previous study which revealed that when levofloxacin was taken orally for 14 consecutive days, the RBC count and Hb content were decreased while the PLT count significantly increased as compared to the control group [23].

Fluoroquinolones cause an increase in the total leukocytic count by inhibiting the development and differentiation of hematopoietic cells. This result is in line with earlier research showing a decline in Hb content, and total erythrocytic count [28]. Similar observations to our study were recorded by previous study who reported that levofloxacin produce a significant decrease in the total erythrocytic count and Hb with increase in platelet counts [23].

Our study allowed us to predict the adverse reactions and the mortality rate with the use of levofloxacin in elderly and the critical ill patients. We demonstrated bilirubin, ALT, AST, creatinine clearance, serum creatinine, hemoglobin, WBC and platelet counts as important variables. It is worth noting that there was no statistically significant variation in random blood glucose (RBG) levels with administration of levofloxacin with critical ill patients having diabetes mellitus.

The strength of this study lies in that it is the only study that was conducted in Saudi Arabia to investigate the impact of levofloxacin side effects in critically ill patients and to evaluate the clinical result after using levofloxacin in a critically ill patients with pneumonia. The small sample size and retrospective nature of the analysis are the main limitations of this study.

CONCLUSION

Due to levofloxacin's widespread use and strong safety record, there may be less reason to suspect that the medication is causing hepatic and renal impairment. Healthcare providers should be informed about the potential for serious liver damage and kidney dysfunction when using levofloxacin in particular or fluoroquinolones in general. Abnormalities in liver enzymes and kidney biomarkers should be taken very carefully because stopping the medication seems to bring about quick improvement. Given the seeming rarity of this side event, it is unclear if routine hepatic and kidney function monitoring is necessary.

REFERENCES

1. M. Bassetti, F. Magnè, D. R. Giacobbe, L. Bini, and A. Vena, "New antibiotics for Gram-negative pneumonia," *European Respiratory Review*, vol. 31, no. 166. 2022, doi: 10.1183/16000617.0119-2022.
2. A. C. Rider and B. W. Frazee, "Community-Acquired Pneumonia," *Emergency Medicine Clinics of North America*, vol. 36, no. 4. pp. 665–683, 2018, doi: 10.1016/j.emc.2018.07.001.
3. O. Paper, "Pneumonia as the Most Common Lower," vol. 67, no. 6. pp. 442–445, 2013.
4. Alshammari, M. K., Alotaibi, M. A., AlOtaibi, A. S., Alosaime, H. T., Aljuaid, M. A., Alshehri, B. M., AlOtaibi, Y. B., Alasmari, A. A., Alasmari, G. A., Mohammed, M. H., Althobaiti, S. M., Almuhaya, R. A., Alkhoshi, T. A., Alosaimi, A. S., & Alotaibi, A. A. (2023). Prevalence and Etiology of Community- and Hospital-Acquired Pneumonia in Saudi Arabia and Their Antimicrobial Susceptibility Patterns: A Systematic Review. Medicina (Kaunas, Lithuania), 59(4), 760. https://doi.org/10.3390/medicina59040760
5. M. K. Alshammari *et al.*, "Prevalence and Etiology of Community- and Hospital-Acquired Pneumonia in Saudi Arabia and Their Antimicrobial Susceptibility Patterns: A Systematic Review," *Med.*, vol. 59, no. 4, pp. 1–15, 2023, doi: 10.3390/medicina59040760.
6. L. A. Mandell *et al.*, "Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the management of community-acquired pneumonia in adults," *Clin. Infect. Dis.*, vol. 44, no. SUPPL. 2, 2007, doi: 10.1086/511159.
7. S. T. Micek, K. E. Kollef, R. M. Reichley, N. Roubinian, and M. H. Kollef, "Health care-associated pneumonia and community-acquired pneumonia: A single-center experience," *Antimicrob. Agents Chemother.*, vol. 51, no. 10, pp. 3568–3573, 2007, doi: 10.1128/AAC.00851-07.
8. C. Cillóniz, A. Torres, and M. S. Niederman, "Management of pneumonia in critically ill patients," *BMJ*, vol. 375, p. e065871, 2021, doi: 10.1136/bmj-2021-065871.
9. Macesic, N., Uhlemann, A. C., & Peleg, A. Y. (2025). Multidrug-resistant Gram-negative bacterial infections. *Lancet (London, England)*, *405*(10474), 257–272. https://doi.org/10.1016/S0140-6736(24)02081-6
10. J. A. Rebuck, D. N. Fish, and E. Abraham, "Pharmacokinetics of intravenous and oral levofloxacin in critically ill adults in a medical intensive care unit," *Pharmacotherapy*, vol. 22, no. 10, pp. 1216–1225, 2002, doi: 10.1592/phco.22.15.1216.33484.
11. Baggio, D., & Ananda-Rajah, M. R. (2021). Fluoroquinolone antibiotics and adverse events. *Australian prescriber*, *44*(5), 161–164. https://doi.org/10.18773/austprescr.2021.035
12. Maitre, T., Godmer, A., Mory, C., Chauffour, A., Mai, T. C., El Helali, N., Aubry, A., & Veziris, N. (2024). Levofloxacin activity at increasing doses in a murine model of fluoroquinolone-susceptible and -resistant tuberculosis. *Antimicrobial agents and chemotherapy*, *68*(11), e0058324. https://doi.org/10.1128/aac.00583-24
13. Roberts JA, Cotta MO, Cojutti P, Lugano M, Della Rocca G, Pea F. Does Critical Illness Change Levofloxacin Pharmacokinetics? Antimicrob Agents Chemother. 2015 Dec 14;60(3):1459-63. doi: 10.1128/AAC.02610-15. PMID: 26666946; PMCID: PMC4775952.
14. V. R. Anderson and C. M. Perry, "Levofloxacin: A review of its use as a high-dose, short-course treatment for bacterial infection," *Drugs*, vol. 68, no. 4. pp. 535–565, 2008, doi: 10.2165/00003495-200868040-00011.
15. P. D. Tamma, S. L. Aitken, R. A. Bonomo, A. J. Mathers, D. Van Duin, and C. J. Clancy, "Infectious Diseases Society of America 2022 Guidance on the Treatment of Extended-Spectrum β-lactamase Producing Enterobacterales (ESBL-E), Carbapenem-Resistant Enterobacterales (CRE), and Pseudomonas aeruginosa with Difficult-to-Treat Resistance (DTR-P. aeruginosa)," *Clin. Infect. Dis.*, vol. 75, no. 2, pp. 187–212, 2022, doi: 10.1093/cid/ciac268.
16. D. N. Fish, "Fluoroquinolone adverse effects and drug interactions," *Pharmacotherapy*, vol. 21, no. 10 II SUPPL. 2001, doi: 10.1592/phco.21.16.253s.33993.
17. C. Jun and B. Fang, "Current progress of fluoroquinolones-increased risk of aortic aneurysm and dissection," *BMC Cardiovasc. Disord.*, vol. 21, no. 1, pp. 1–10, 2021, doi: 10.1186/s12872-021-02258-1.
18. J. Segreti, "A multicenter, randomized study comparing the efficacy and safety of intravenous and/or oral levofloxacin versus ceftriaxone and/or

cefuroxime axetil in treatment of adults with community-acquired pneumonia," *Infect. Dis. Clin. Pract.*, vol. 7, no. 2, pp. 88–89, 1998, doi: 10.1097/00019048-199802000-00005.
19. T. Neto Gonçalves, D. Sousa, N. Marto, and A. B. Horta, "Levofloxacin-Induced Acute Pancreatitis," *Cureus*, vol. 13, no. 2, pp. 12–14, 2021, doi: 10.7759/cureus.13301.
20. Rissardo, J. P., & Caprara, A. L. F. (2023). Fluoroquinolone-Associated Movement Disorder: A Literature Review. *Medicines (Basel, Switzerland)*, *10*(6), 33. https://doi.org/10.3390/medicines10060033
21. Y. Hirano *et al.*, "Toxic epidermal necrolysis induced by tirabrutinib," *J. Dermatol.*, vol. 49, no. 4, pp. e135–e136, 2022, doi: 10.1111/1346-8138.16274.
22. A. A. Khan, U. Aisha, A. Hassan, Z. Haider, and D. E. Cook, "Levofloxacin-Induced Toxic Epidermal Necrolysis," *Cureus*, vol. 15, no. 5, pp. 4–9, 2023, doi: 10.7759/cureus.39504.
23. Anita Karim, Shahid Ahmed, Leonard J. Rossoff, Rina K. Siddiqui, Harry N. Steinberg, Possible Levofloxacin-Induced Acute Hepatocellular Injury in a Patient with Chronic Obstructive Lung Disease, Clinical Infectious Diseases, Volume 33, Issue 12, 15 December 2001, Pages 2088–2090, https://doi.org/10.1086/338156
24. ABD EL FADIL, H., M. MAHMOUD, N., & MOHAMED ABD EL-MOTTLEB, D. (2020). AMELIORATIVE EFFECT OF VITAMIN E AGAINST SOME ADVERSE EFFECTS OF LEVOFLOXACIN IN MALE RATS. Assiut Veterinary Medical Journal, 66(165). https://doi.org/10.21608/avmj.2020.166394
25. Clark, P. (2002). Fundamentals of Veterinary Clinical Pathology. Australian Veterinary Journal, 80(12). https://doi.org/10.1111/j.1751-0813.2002.tb11349.x
26. Daugirdas, J. T. (2018). Handbook of chronic kidney disease management. In Handbook of Chronic Kidney Disease Management. https://doi.org/10.12968/jorn.2011.3.4.204
27. Ferguson, M. A., & Waikar, S. S. (2012). Established and emerging markers of kidney function. In Clinical Chemistry (Vol. 58, Issue 4). https://doi.org/10.1373/clinchem.2011.167494
28. Ahmed, M. H., Resen, A. K., & Al-Niaeem, K. S. (2022). Effects of antibiotic residues on some health parameters of Planiliza abu H. in Shatt Al-Arab, Southern Iraq. Caspian Journal of Environmental Sciences, 20(5). https://doi.org/10.22124/cjes.2022.6080
29. Memon, N., Weinberger, B. I., Hegyi, T., & Aleksunes, L. M. (2016). LiverTox: Clinical and Research Information on DrugInduced Liver Injury [Internet]. In Pediatr Res. (Vol. 176, Issue 1).
30. Karim A, Ahmed S, Rossoff LJ, Siddiqui RK, Steinberg HN. Possible levofloxacin-induced acute hepatocellular injury in a patient with chronic obstructive lung disease. Clin Infect Dis. 2001;33:2088–90.